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Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL.,

PETITIONERS,

v.

WESTERN STATES MEDICAL CENTER, *ET AL.*,

RESPONDENTS.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

BRIEF OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENTS

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INTEREST OF AMICUS CURIAE [1]

The American Pharmaceutical Association ("APhA") is the national, professional society of pharmacists. It is a voluntary membership organization of over 50,000 individuals, including pharmacists, pharmaceutical scientists and pharmacy students. Its pharmacist members are engaged in virtually every area of pharmacy practice, including independent and chain community pharmacy practice, hospital pharmacy practice, nuclear pharmacy practice, long term care pharmacy practice, home health care practice and hospice practice. Members are also involved in academia and some work for pharmaceutical manufacturers. While it is not possible to quantify the actual number of APhA's members who engage in drug compounding activities on a regular basis, virtually all practicing pharmacists will be involved with compounding activities at some point during their career.

APhA has a compelling interest in ensuring a pharmacist's right to compound drug formulations to meet the needs of patients, in collaboration with practicing physicians,[2] as part of the health care giving team. Pharmacists' compounding activities are a critical component of the American health care system, allowing physicians to prescribe medication therapy to best meet the needs of their patients. APhA submits this brief to protect the interests of its members, the interests of all pharmacists who now, or in the

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[1] Petitioners and Respondents have consented to the filing of this brief *amicus curiae*. The consents have been filed with the Clerk of this Court. No part of this brief has been authored by counsel for either party. No persons other than the *amicus curiae*, its members or their counsel made a monetary contribution to the preparation and submission of this brief.

[2] Physicians do not have an exclusive domain in prescribing medications: dentists, advanced practice nurses, physician assistants and other health professionals may also prescribe medications in some states. The term "physician" is used in this brief to refer to physicians and other health care professionals with privileges and responsibilities related to prescribing drug therapy.

future may, engage in the practice of compounding drugs to meet the needs of their patients and the requirements of the physician, all in furtherance of the physician/pharmacist/patient relationship. We hope in this brief to highlight the importance and major contribution that compounding by the pharmacy profession brings to the drug delivery and medication use process in the United States.

SUMMARY OF ARGUMENT

Compounding of medications for patient use has been a significant component of the practice of pharmacy and medicine since time immemorial. It has traditionally been characterized by the physician/pharmacist/patient relationship wherein professionals work together to individualize care for the maximum benefit of the patient. Compounding is performed by a licensed pharmacist, physician or other qualified health care professional. It has routinely involved the formulation of individualized treatment in response to a valid prescription from a physician or in response to a reasonably anticipated prescription based upon prior experience and expected needs of individual patients. Pharmacy compounding is performed on the site of the pharmacy for nearly immediate dispensing and use by, or administration to, the patient. The profession's definition of compounding does not encompass the preparation of massive amounts of a drug product with the contemplation of distribution to a mass market of unknown users in unknown venues.

These characteristics of pharmacy compounding were extant when Congress passed the Food, Drug and Cosmetic Act in 1938 ("FDCA"), 21 U.S.C. § 301 *et seq.*, and there was no contemplation in the legislative history that compounding would be limited or prohibited as a result of that statute. In fact, compounding continued without benefit of "authorizing legislation" until 1997 when the traditional characteristics of compounding were codified in the Food and Drug Administration Modernization Act of 1997 ("FDAMA"). 21

U.S.C. § 353a. The significant differences were that FDAMA contained the limitation that prohibited advertising of specific compounded products, and volume limits on products distributed out of state. It is the advertising limitation that is in issue in this case.

The FDCA and the processes it mandates were designed to address the situation where a "new drug" would be developed over time, proved as to its safety and then mass marketed to millions of people throughout the United States.[3] There is an obvious conflict between this concept of a "new drug" and a compounded drug. A compounded drug is one that is formulated for a specific patient need, such as an allergy to an ingredient, that cannot be met by a mass manufactured drug. A compounded drug is used fairly promptly after it is formulated. Because of the limited and specific nature of the compounded formulation, it simply would not be possible for a compounded drug to go through the "new drug" approval process that takes years to accomplish with the expenditure of a large amount of money. To have applied the "new drug" requirements of FDCA to the process of compounding from 1938 going forward would have been tantamount to outlawing compounding, and this, clearly, was neither intended nor occurred.

It is unfounded to suggest that traditional compounding, as detailed above, offers a realistic opportunity to do an "end run" around the "new drug" regulatory system. Even including all compounded drugs in all settings nationwide (hospitals, long-term care facilities, community pharmacies, etc.), compounded drugs account for a very small percent of the total dispensed drugs in the United States. It makes no

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[3] Subsequent amendments to the act expanded the requirements of a "new drug" to include efficacy. 21 U.S.C. §§ 201(p)(1) and (2); 21 U.S.C. § 355(b), (d) and (e). There existed legislation exempting pharmacists from registration and inspection which further indicates that compounding was not contemplated within the definition of "new drug." *See* 21 U.S.C. § 360(g)(1) and 21 U.S.C. § 374(a)(2)(A).

logical sense to claim, as the government does, that the only distinction between compounding and manufacturing is the limit on the pharmacist's right to advertise a particular prescription drug that he or she is able to compound. This single criterion does nothing to further any governmental interest, especially not its stated concern that without this limitation, pharmacists will be able to do an "end run" around the regulatory process.

Compounding was not illegal before the passage of FDAMA,[4] and is regulated by states as part of their oversight of the practice of pharmacy. While FDAMA attempted merely to codify what pharmacists were already doing in the compounding arena, it introduced for the first time the legally imposed limitation that advertising was not allowed. Pharmacists should not be required to forego their constitutional rights in order to continue to engage in the activities they have been legally engaging in for centuries.

STATEMENT OF FACTUAL CONSIDERATIONS

I. The Practice of Pharmacy

In most communities, pharmacists are the primary providers of pharmaceuticals and pharmaceutical care services to the American public. The critical function that pharmacists provide to patient health care is serving as the medication use specialist whose services increase the effectiveness of drug therapy. Pharmacists fulfill a societal need by increasing the effectiveness of drug therapy and thereby improving patient health outcomes. Moreover, pharmacists are the most accessible health-care professionals and enjoy a high degree of earned trust by the public.

Practicing pharmacists, through their education and licensure, assume an ethical obligation to the public to

[4] The fact that the government makes the argument that compounding was not illegal during the period from 1938 to 1997 because of FDA's *noblesse oblige* is unfounded.

maximize the intended benefits of drug therapy while minimizing the risk of unintended side effects and adverse reactions. In preparing a medication for dispensing, the pharmacist assesses the patient's condition, the appropriate dosage scheduling, and any contraindications of the medication with the patient's other prescriptions or diseases. The pharmacist may provide the patient with information on the potential risks and benefits of the medication and assess the patient's understanding of the prescription instructions in order to achieve an optimal therapeutic outcome.

Pharmacists have the responsibility to deliver to patients individualized packages of medication containing patient-specific instructions, an appropriate quantity of the medication, and essential product information that will allow the patient to use the medication most effectively. Pharmacists have expanded from primarily a product-oriented function, focusing on the accurate production and dispensing of the drug product, to a patient-oriented focus, emphasizing proper use of drug therapy by the patient. Today, pharmaceutical care necessitates a proactive healthcare provider who assumes interactive and participatory responsibilities with the intention of improving outcomes. When manufactured products are not appropriate for a patient, the pharmacist's efforts to provide pharmaceutical care are thwarted unless compounding is an option. Without pharmacy compounding, there would be no medication to dispense, nor any medication therapy to optimize. Compounding enables pharmacists to contribute their medication knowledge and expertise to produce individualized medications that meet these needs and improve health outcomes.

II. Pharmacy Compounding

As a component of monitoring the distribution and use of prescribed drug products, pharmacists compound prescriptions to meet the specific needs of individual patients. Compounding has always been a basic part of pharmacy practices; the drugs, dosage forms, and equipment or techniques have changed as pharmacy practice has advanced.

As A.C. Wooten in *Chronicles of Pharmacy* said, "[p]harmacy, or the art of selecting, extracting, preparing and compounding medicines from vegetable, animal, and mineral substances, is an acquirement that must have been almost as ancient as man himself on earth."[5] The early practice of pharmacy required the compounding of virtually all medications, because there were few, if any, commercially available products. As pharmaceutical companies were founded there became less need for compounding most widely used products, although the need to compound has certainly not disappeared.

Compounding may involve different activities in different pharmacy practice settings. It may mean the preparation of oral liquids, topicals, suppositories; the conversion of one dose or dosage form into another; the preparation of select dosage forms from bulk chemicals; the preparation of intravenous admixtures, parenteral nutrition solutions, pediatric dosage forms from adult dosage forms; the preparation of radioactive isotopes; or the preparation of cassettes, syringes, and other devices with drugs for administration in the home setting. Examples of some of the most common compounded products include lotions, ointments, creams, gels, suppositories, intravenously administered fluids and medications, total parenteral nutrition products, oral suspensions, and troches.

Physicians and pharmacists recognize that some individuals and their healthcare needs do not always fall in the windows of commercially available dosage strength and formulations and that large-scale manufacturers cannot tailor-make a medication for a single patient or a handful of patients in a cost effective manner. Many patients need custom-made medication dosages to solve specific medical problems. Pediatric or geriatric patients may need extremely small

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[5] Wooten, A.C., *Chronicles of Pharmacy, quoted in* Dinah G. Jordan, *Pharmacist Compounding v. Veterinarian Compounding: Similarities and Differences,* 205 JAVMA 256 (1994).

doses, cancer patients may need specific combinations of chemotherapy drugs to treat their disease, or special dosage forms may be necessary to care for patients with AIDS, chronic pain or other maladies.[6] Some therapies, such as parenteral nutrition, can only be provided to patients using compounded dosage forms. Still other patients need preservative-free products, liquids with special flavors, or delivery systems that are not commercially available.

Some therapies, such as hyaluronidase injection (used to increase dispersion and absorption of other drugs injected under the skin), must be compounded because they generate insufficient revenue to pharmaceutical companies to justify large-scale manufacturing. Additionally, some medications may not have sufficient shelf life to withstand the commercial distribution process and therefore need to be prepared at the time of dispensing, such as radioactive drugs used to diagnose or treat disease. Many manufactured "finished pharmaceutical" products are only "finished" in the sense of being ready to ship and then store in the pharmacy. The products must still be compounded to provide a dosage form suitable for a patient's treatment.

It is a fundamental right of the pharmacy profession to extemporaneously compound quality prescription products for patients who have unique medication needs. The pharmacist may, through understanding of the principles of compounding, recommend drug therapy that is not provided by the pharmaceutical industry but that is individualized for a specific patient's needs at a specific time. For these unique needs, many pharmacists offer compounding services guided by the Good Compounding Practices established by the U.S.

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[6] The pharmaceutical manufacturers recognize the need for compounding, because they include instructions for compounding specialized dosage forms, such as oral suspensions, in some of their package inserts, which are the instructions for use that accompany any drug product and must be approved prior to distribution by the FDA.

Pharmacopoeia.[7] In providing compounding services, pharmacists work hand-in-hand with physicians to solve problems not addressed by commercially available drugs, and develop a special and unique relationship with the patients they serve.

III. Types of Compounding

Pharmacists possess the unique knowledge and skill required for compounding and preparing medications to meet the unique and immediate needs of a patient. Extemporaneous compounding allows pharmacists the opportunity to use their scientific education and training to individualize patient care through the preparation of patient-specific products.

There are many different circumstances calling for compounded prescriptions, including the isolated, the routine and the batch prepared. The isolated prescription is one that the pharmacist is not expecting to receive nor expecting to dispense again.[8] The routine prescription is one the pharmacist may expect to receive in the future on a routine basis, and there may be some benefits to product quality to standardize these preparations, i.e., preparation protocols on file.[9] The batch-prepared prescription is one in which multiple identical units are prepared as a single operation in anticipation of the receipt of prescriptions.[10] All of these compounding activities have been part of the pharmacy profession for many years.

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[7] *Pharmacy Compounding Practice & Sterile Drug Products for Home Use*, Rockville, Maryland: U.S. Pharmacopeia, 1996. The U.S. Pharmacopoeia is an official compendium of drug information recognized by the FDCA.

[8] 21 U.S.C. § 503a (a)(1)(A) and (B).

[9] 21 U.S.C. § 503a (a)(2)(A).

[10] 21 U.S.C. § 503a (a)(2)(B).

A. Compounding in Cancer Treatment

One of the most important clinical needs for compounding occurs in the care of patients with cancer. Almost all chemotherapy involves drugs and drug combinations that are compounded by pharmacists. It is imperative that a patient receive the correct drug dosage based upon the patient's body size, the type of cancer, the size and type of tumor, and the clinical condition of the patient. This can only be accomplished using compounded patient-specific medication preparations.

B. Compounding for Pediatric Patients

The compounding of pediatric dosage forms has also been an area of extensive activity, particularly in pediatric hospitals, because many drugs used in pediatric treatment are not available in dosage forms appropriate for pediatric patients. Consequently, commercial products manufactured for use in adults must be modified and compounded for use in children. It has been estimated that more than 40% of doses given in pediatric hospitals require compounding to prepare a suitable dosage form. Indeed, utilization of compounded medications is essential for the provision of medical care to hospitalized children.

C. Compounding in Hospitals

In the hospital setting, one of the biggest challenges is to provide individualized dosages specifically directed to the unique needs of each patient. Extemporaneous compounding services within the hospital pharmacy allow the hospital's physicians, nurses and pharmacists to meet this challenge. In particular, intravenous admixtures are compounded because they need to be highly individualized and facilitate administration of drugs not suitable for other routes of administration. It is not practical for a manufacturer to make numerous slightly different products to address the entire range of patients' needs. Generally, only a few or even one dosage form will be commercially viable. However, the commercial form could be used in compounding the myriad

of concentrations and combinations used to meet patients' needs in the hospital setting.

Hospital pharmacists have always utilized their compounding skills to serve the needs of their patients. Because daily intravenous therapy is provided through compounding of medications, nearly every person who has ever been admitted to a hospital has received a compounded product, including those patients receiving outpatient surgery. In fact, the immediate availability of extemporaneous compounding provides the hospital physician with literally any form or strength of medication needed for a specific situation.

D. Compounding in Hospice Care

Hospice programs provide care for patients near the end of their lives. The goal is to enable each patient to make the choices that will provide the best quality of life during the last weeks or months of life. It is a special type of care designed to assist patients to carry on their lives comfortably by managing symptoms, controlling pain, and allowing them to spend their last days with dignity either at home or in a home-like setting. The compounding component of pharmaceutical care is a natural component of hospice care resulting in an enhanced quality of patient care.

Hospice services are for patients who can no longer benefit from curative treatment and generally have a life expectancy of six (6) months or less. About 60% to 70% of hospice patients have cancer and experience debilitating, intractable pain, severe anxiety and depression and have social, psychological, and financial concerns. Hospice pharmacists devise drug therapy protocols that establish optimal pain and symptom control often using compounded dosage forms and enhance patient compliance through patient

education, and monitor patient outcomes in a supportive and humanistic fashion."

Medications to alleviate pain and to control nausea and vomiting are the most common prescriptions for patients in the hospice setting. If commercial products that provide the precise dose(s) required are not available, they can often be supplied by extemporaneous compounding. Patient-specific formulations and dosage forms are constantly being developed by compounding pharmacists to meet the needs of these patients. One of the problems for many hospice patients is that pain medications are not manufactured in the required dosages. Additionally, patients often are not physically capable of swallowing the number of commercially manufactured tablets required. A pharmacist can compound a stronger product by transforming a tableted dosage form into a liquid that is easily swallowed. Often patients cannot take any medication by mouth, and often their veins are not accessible to inject medications. In these situations, physicians and pharmacists must modify traditional medications into products that may be applied topically or delivered rectally. Pharmacists engaged in compounding are important in hospice care and their role will undoubtedly continue to evolve and expand in the future.

IV. Preparation of Compounded Pharmaceuticals-Regulatory Changes

The practice of pharmacy has been historically regulated at the state level. Traditional compounding has been considered an integral part of the practice of pharmacy, and therefore, has been appropriately regulated by state boards of pharmacy. A review of state laws reveals that all 50 states

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[11] *Hospice Care and the Pharmacist,* 1 International Journal of Pharmaceutical Compounding 11 (January/February 1997).

and the District of Columbia describe compounding in their pharmacy practice laws. [12]

NABP's Model State Pharmacy Act defines "practice of pharmacy" to include compounding of drugs and devices. Specifically, "practice of pharmacy" is the:

> "[I]nterpretation, evaluation, and implementation of Medical Orders: the Dispensing of Prescription Drug Orders; participation in Drug and Device selection, Drug Administration, Drug Regimen Reviews...and the responsibility for Compounding and Labeling of Drugs and Devices..."[13]

The Model Act defines "compounding" in terms of preparation of drugs and devices:

> "Compounding" means the preparation, mixing, assembling, packaging, or Labeling of a Drug or Device (i) as the result of a Practitioner's Prescription Drug Order or initiative based on the practitioner/patient/pharmacist relationship in the course of professional practice, or (ii) for the purpose of, or as incident to, research, teaching, or chemical analysis and not for sale or Dispensing. Compounding also includes the preparation of Drugs or Devices in anticipation of Prescription Drug Orders based on routine, regularly observed prescribing patterns."[14]

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[12] See *NABPLAW® Pharmacy law database, NABP's database of state pharmacy practice acts and regulations.*

[13] Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy, § 104 (1998).

[14] *Id.*, § 105(f).

The Model Act associates compounding with a "prescription drug order," which is defined as "a lawful order from a Practitioner for a Drug or Device for a specific patient."[15]

Most state boards of pharmacy are in the process of or have completed full revisions of their pharmacy practice acts to expand the role of pharmacists.[16] These changes have given pharmacists the opportunity to engage in innovative practices and to promote patient health. Through their pharmacy practice laws, states recognize and regulate compounding as part of the practice of pharmacy.

In short, statutes and regulations are enacted in every state to deal effectively with compounding as part of pharmacy practice. Restricting free speech will not add to the effectiveness of these statutes and regulations any more than it would add to the government's enforcement arsenal in this case. The proposed solution and the problem are simply unrelated.

ARGUMENT

I. Compounding Is Not Manufacturing

At the very heart of the dispute giving rise to this case is the apparent confusion in trying to determine the difference between compounding and manufacturing. Compounding has been defined by the National Association of Boards of Pharmacy ("NABP"):

> **Compounding** - The preparation, mixing, assembling, packaging, or labeling of a drug or device (i) as the result of a practitioner's

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[15] The NAPB *Good Compounding Practices Applicable to State Licensed Pharmacies* includes a provision restricting a pharmacist's solicitation of specific drug products. However, such a state level provision does not make the advertising prohibition Constitutionally defensible.

[16] Knowlton, C.H., *J APhA* 1997; NS 37 (3):361.

> Prescription Drug Order or initiative based on the pharmacist/patient/prescriber relationship in the course of professional practice or (ii) for the purpose of, as an incident to research, teaching, or chemical analysis and not for sale or dispensing. Compounding also includes the preparation of drugs and devices in anticipation of Prescription Drug Orders based on routine, regularly observed patterns.[17]

Stated simply, the purpose of compounding by a pharmacist is to prepare an individualized drug treatment for a patient based on an order from a duly licensed prescriber. Manufacturing of a drug is defined as follows:

> **Manufacturing** - The production, preparation, propagation, conversion or processing of a Drug or Device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis, and includes any packaging or repackaging of the substance(s) or Labeling or relabeling of its container, and the promotion and marketing of such Drugs or Devices. Manufacturing also includes the preparation and promotion of commercially available products from bulk compound for resale by pharmacies, Practitioners, or other Persons.[18]

The fundamental difference between compounding and manufacturing is the existence of a pharmacist/ prescriber/patient relationship that controls the preparation of the drug product. Compounded drugs are not for resale, but rather, are personal and responsive to the patient's immediate needs. They are produced and administered by the patient's health care professionals, which allows for the monitoring of

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[17] *Good Compounding Practices Applicable to State Licensed Pharmacies*, Subpart A. Park Ridge, IL:NABP, 1993.

[18] *Id.*

patient outcomes. The compounded drug may be assigned a very short expiration date and the pharmacist may personally advise his patients to immediately report any physical change in the compounded prescription as well as any adverse reactions.

On the other hand, drug manufacturers produce batches consisting of millions of dosage units, such as tablets or capsules, for resale utilizing many personnel and large scale manufacturing equipment. These products are distributed through the normal channels of interstate commerce to individuals unknown to the company. Manufactures are not required to, and do not, provide oversight of individual patients. Federal regulation of large-scale commercial manufacturing is intended to prevent the production of large quantities of ineffective or dangerous manufactured drugs and have them introduced into commerce. Because of the absence of a close relationship with a physician and patient, the manufacturer may remain unaware of a drug's negative effect upon the patients to whom it is administered until larger numbers of adverse effects appear. It is these differences, not advertising, that distinguish compounding from manufacturing.[19]

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[19] We recognize that the definition of manufacturing includes "promotion" of drug products, whereas the definition of compounding does not. We submit that this does not, however, lead to a valid conclusion that promotion of either compounding or a compounded drug product turns the activity of compounding into manufacturing. Of those states that have adopted some form of the Model Act, only ten (10) include "promotion and marketing" as part of their definition of manufacturing. Alaska Stat. § 8.80.480; Ga. Code Ann. § 26-4-5(23); La. Rev. Stat. Ann. § 1164; Miss. Code Ann. § 73-21-73(q); N.H. Rev. Stat. Ann. § 318.1 (VIII); N.M. Stat. Ann. § 61-11-2.Q.; Okla. Stat. tit. 59, § 353-1(20); S.C. Code Ann. § 40-43-30(29); Tenn. Code Ann. § 63-10-404(18); W. Va. Code Ann. § 30-5-1b(o).

The fundamental differences between manufacturing and compounding are further demonstrated by additional NABP Model Rules, parts of which were eventually codified into the FDAMA of 1997. The NABP Model Rules provide the following:

> "Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions that have been generated solely within an established pharmacist/patient/prescriber relationship, and provided that they maintain the prescriptions on file for all such products compounded at the pharmacy (as required by State law). The compounding of inordinate amounts of drugs in anticipation of receiving prescriptions without any historical basis is considered *manufacturing*...
>
> ...The distribution of inordinate amounts of compounded products pursuant to a legitimate prescription out of state without a prescriber/patient/pharmacist relationship is considered *manufacturing*. Pharmacists engaged in the compounding of drugs shall operate in conformance with applicable State law regulating the practice of pharmacy."[20]

The relationship between the compounding pharmacist and the practitioner provides an appropriate system of checks and balances to make sure that the patient's health is protected and served. A legally compounded prescription by a pharmacist always is authorized by a prescriber. The pharmacist acts as a valuable resource for determining drug compatibility, dosage formulation, etc., to meet the patient's needs and prescriber-intended outcomes, and when

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[20] *Good Compounding Practices Applicable to State Licensed Pharmacies*, Subpart A, Park Ridge, IL:NABP, 1993. [Emphasis added] (*See also*, 21 U.S.C. § 503a (a)(2)(A) and (B)).

appropriate, may refuse to dispense a prescription calling for compounding that cannot be safely performed. This relationship is the basic difference between compounding and manufacturing, not advertising.

Prior to promulgation of their Compliance Policy Guidelines in the early 1990s and the subsequent enactment of FDAMA, the FDA rarely asserted that compounding was manufacturing. The relevant provisions of FDAMA were promulgated to clarify the inapplicability of the FDCA to compounding.[21] In its brief, the government cites a number of court decisions that, it alleges, equate the traditional compounding of drugs to the manufacturing of "new drugs." *See* Petitioners' Brief at pp. 5 and 6. As the facts in these cases make clear, however, traditional compounding was never at issue in these cases and nor was it ever equated with manufacturing.

In both *United States v. 9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988), and its companion case, *U.S. v. Algon Chemical, Inc.* 879 F.2d 1154 (3rd Cir. 1989), the courts addressed the issue of misbranding of bulk drugs. The misbranding resulted from the fact that the drug labels did not contain "adequate directions for use." The FDA claimed, and both courts concurred, that this misbranding made distribution of the drugs to veterinarians for compounding and use in their practice illegal, so the drugs could be seized by the FDA. In both cases, the courts enjoined the sale of the "misbranded" bulk animal drugs intended for use in compounded veterinarian drug products. *Id.*

It is important to note that neither court decision directly addressed the issue whether the traditional compounding of drugs by pharmacists and physicians equals manufacturing that is "subject to the FDCA's premarket approval process" as contended by the government. See Petitioners' Brief, p. 5. On the contrary, both courts explicitly confirmed the authority

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[21] S. Rep. No. 43, 105th Cong., 1st Sess., 67-68 (1997).

of a practitioner to compound legally acquired drugs, free from registration and inspection requirements, in the course of his practice. *Algon Chemical*, 879 F.2d at 1160; *Containers*, 854 F.2d at 177, 178.

In another case relied upon by the government, *United States v. Baxter Healthcare Corp.*, 901 F.2d 1401 (7th Cir. 1990), the FDA successfully challenged a program, operated by a recognized drug manufacturer through its regional drug preparation center, involving the reconstitution, repackaging, freezing, and distribution of already approved drugs to healthcare providers without specific FDA approval for the manufacturing of "new drugs." In analyzing the pertinent facts, the court determined that the respondents, by transforming powders and concentrates on a large scale into dosage packages that were not prepared pursuant to a patient-specific prescription and were suitable for immediate use by healthcare providers without further reconstitution or dilution, were operating a manufacturing operation that required "new drug" approval from the FDA. *Id.* In *Baxter Healthcare*, the court was not faced with the issue of traditional compounding of drugs by pharmacists or physicians, but rather, it was faced with the clear manufacturing of drugs subject to FDA regulation.

In reaching its conclusion, the court noted the distinction drawn by Congress between the commercial manufacturing of drugs and the reconstituting (or compounding) of drugs performed by pharmacists and physicians. *Baxter Healthcare*, 901 F.2d at 1409, 1411. The court noted that Congress, through the FDCA, intended to protect the traditional compounding of drugs from FDA regulation by saying:

> "As a policy choice, Congress has exempted pharmacies and physicians from the registration and inspection requirements that apply to all manufacturers of drugs. 21 U.S.C. §§ 360(g)(1), (2), 374(a)(1), (2). The FDA only follows that lead by focusing on the mass commercial distribution of drugs rather than at the individual level of hospitals

> and pharmacists. This does not suggest that the FDA has taken a path which is 'manifestly contrary to the statute,' *Chevron*, 467 U.S. at 844, 104 S.Ct. at 2782, but to the contrary suggests sound adherence to congressional intent."

Id. at 1411.

In *Professionals and Patients for Customized Care v. Shalala*, 56 F.3d 592 (C.A. 5 (Tex.), 1995), the court was called upon to address the issue as to whether the FDA's Compliance Policy Guide constituted a substantive rule of law issued by the agency without benefit of the Administrative Procedure Act, or whether it was, as billed, a policy guide. Both the lower court, *Professionals and Patients for Customized Care v. Shalala*, 847 F.Supp. 1359 (S.D. Texas, 1994), and the appellate court, *Professionals*, 56 F.3d 592 (C.A. 5 (Tex.) 1995), concurred that it was nothing more than an internal guide for the FDA's enforcement efforts. The governments citation of this case at the appellate level for the proposition that "compounded drugs are 'new drugs' subject to the FDA's premarket approval requirements" seems to overstate the holding in the case. In fact, the footnote referred to by the government merely points out that the FDCA does not exempt pharmacies or compounded drugs from its provisions. The court did note that the FDA has not historically brought enforcement actions against pharmacies engaged in traditional compounding, while at the same time, the court recognized that pharmacies that practice traditional compounding are regulated primarily by the states and are exempt from FDA registration requirements and inspections. *Professionals*, 56 F.3d at 594 (*see also* 21 U.S.C. § 360(g)(1) and 21 U.S.C § 374 (a)(2)(A)).

On the other hand, the facts in *United States v. Sene X Eleemosynary Corp.*, 479 F.Supp. 970 (S.D. Fla. 1979), clearly demonstrate a situation where a "manufacturer" is trying to look like a traditional pharmacy and failed to do so. In that case, a corporation compounded a line of products as its only "pharmacy" activity, and distributed those products

interstate in large quantities without the existence of any real pharmacist/patient/physician relationship. Prescriptions were written and delivered by mail from physicians unknown to the patient. Without resolving whether customary or usual acts of pharmacy were exempt from the FDCA's "new drug" provisions, the court swiftly determined that the corporation's actions did not constitute the practice of pharmacy by saying:

> "The question of whether the customary or usual practice of pharmacy is exempt from the Act's new drug provisions need not be resolved in this case, for the means by which the defendants compound, promote, and ultimately distribute GH-3 constitute something wholly apart from the normal practice of pharmacy."

Id. at 978.

As the case law cited by the government makes clear, no court has held that the traditional compounding of drug products by a pharmacist or physician constitutes the manufacturing of drugs subject to FDCA regulation. The government has not and cannot put forth case law that involves the type of traditional compounding at issue in this case.

II. A Compounded Drug Product is not a "New Drug" as Contemplated in FDCA & FDAMA

Compounding of drug products by pharmacists and physicians does not constitute the manufacturing of "new drugs." Historically, while the FDA has subjected "new drugs" to its stringent statutory requirements, pharmacists have continued the traditional compounding of drugs without interference from the FDA. In its Petition, however, the government takes a quantum leap by equating the advertisement of a prescription drug product with manufacturing. *See* Petitioners' Brief at pp. 14, 15. It claims that a pharmacist's advertisement of a specific compounded drug automatically transforms that pharmacist into a manufacturer of "new drugs." While the government clearly

grasps the value and essentials of compounding, it now claims that the advertising of particular compounded drugs creates a loophole in the "new drug" approval process, and therefore, that such activity must be subject to all of FDA's new drug regulations. *See* Petitioners' Brief at pp. 24-26, 32-37, 40, and 41. The government's argument is completely lacking in merit.

A. The Federal Food, Drug & Cosmetic Act of 1938

Congress adopted the Federal Food, Drug & Cosmetic Act in 1938 ("FDCA") to regulate the sale of manufactured drugs to the general public. 21 U.S.C. § 301 *et seq.* As part of this legislation, no 'new drugs' could be introduced into interstate commerce unless they first underwent testing and were approved as safe by the FDA. Section 505(a) of the 1938 regulation (later codified as 21 U.S.C. § 355(a)) provided that: "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an application filed pursuant to subsection (b) is effective with respect to such drug." There is no indication that Congress, the states, pharmacists, or the FDA in 1938 or in the decades that followed believed that compounding of a drug by a pharmacist constituted the introduction of a 'new drug' into the marketplace, regardless of whether the drug was given to the patient in the pharmacy or mailed via interstate commerce to an individual patient. We contend that this is for obvious reasons.

At the time the Act was adopted, there were not very many manufactured drugs available, though the prevalence of manufactured drugs was on the increase. It was, in fact, this increased prevalence of manufactured drugs, as compared with compounded drugs, that formed, at least in part, the impetus for enactment of the FDCA. Following adoption of the FDCA, pharmacists continued to compound without submitting new drug applications. The FDA did not attempt to impose the new drug application requirements upon such pharmacy compounding. Indeed, as a practical matter, given the stringency of new drug application requirements, the

relatively large patient population, and the substantial time and monetary investment required, it would have been all but impossible for pharmacists to meet those requirements had they attempted to do so.

Accordingly, the lack of evidence to the contrary suggests that no one in 1938 viewed section 505 of the FDCA as placing any limitation on compounding. If compounded drugs were to be subjected to the "new drug" requirements of the FDCA, this would have been tantamount to the outlawing of compounding, and the supply of compounded medications to the American public would have been brought to a virtual halt. It is inconceivable that Congress intended to deem all compounding to be illegal, and it is even more unlikely that Congress would have taken this drastic step without explicitly saying so.

B. The Food and Drug Administration Modernization Act of 1997

In 1997, FDAMA was enacted, essentially codifying the general practices involved in compounding that had taken place for many years. FDAMA recognizes the value of compounding and continues to permit pharmacists to compound drugs under the same conditions as traditionally recognized by state regulators and the FDA. FDAMA requires, in relevant part, that: 1) compounding be performed by a licensed pharmacist or physician for the benefit of an identified patient and a) be based upon a valid, unsolicited prescription from a practitioner licensed to prescribe drugs; or b) compounded in limited quantities before receipt of a valid prescription order based upon a history of receiving valid prescription orders from an established pharmacist/physician/patient relationship. 21 U.S.C. § 353a (a); and 2) the pharmacist does not compound regularly or in inordinate amounts drug products that are essentially copies of a commercially available drug product. 21 U.S.C. § 353a(b)(1)(D).

The new conditions, in relevant part, that FDAMA places upon the compounding of drugs that were not a part of "traditional compounding" include: 1) the pharmacist may "not advertise or promote the compounding of any particular drug, class of drug, or type of drug," *see* 21 U.S.C. § 353a(c); 2) the compounded drug product may not be a drug product that presents difficulties for compounding that would adversely affect safety or efficacy, *see* 21 U.S.C. § 353a(b)(3)(A); and 3) the pharmacist or physician may distribute interstate only limited quantities of compounded drugs, *see* 21 U.S.C. § 353a(b)(3)(B).

Contrary to the government's assertion, the new advertising limitation in FDAMA should not transform the compounding of a prescription drug product into the manufacturing of a "new drug." Certainly, there is a substantial government interest in precluding persons or organizations from avoiding the stringent approval process for new drugs by claiming they are merely compounding. As described above, it defies logic to contend that this interest is in any way advanced by limiting the right of a pharmacist in the lawful exercise of his profession to advertise the availability of a particular compounded drug product.

Surrendering a constitutional right should not be the price one has to pay in order to meet the government's substantial interest of avoiding "end runs" around the "new drug" regulatory process. FDAMA includes numerous conditions on the practice of compounding that directly and realistically address the true features of compounding and are more than sufficient to meet the government's objectives in preventing the subversion of the "new drug" approval requirements. FDAMA specifically requires that a compounded drug product be comprised from a list of approved drug substances, *see* 21 U.S.C. § 353a(b)(1); and restricts the compounding of a drug product that has been removed from the market because it has been determined to be unsafe or not effective, *see* 21 U.S.C. § 353a(b)(1)(C). The Act further restricts a compound drug product identified

by regulation as presenting difficulties for compounding that would adversely affect safety or efficacy, *see* 21 U.S.C. § 353a(b)(3)(A).

The government contends in its brief that advertising is the primary indicia of manufacturing as compared to compounding. *See* Petitioners' Brief at pp. 14-16; 33-35. We contend on the contrary that advertising is not the linchpin that, standing alone, can turn compounding into manufacturing. In fact, advertising of a specific compounded product is totally neutral to the issue of compounding versus manufacturing.

CONCLUSION

For the reasons stated above, the Court should declare the solicitation and advertising prohibitions contained in 21 U.S.C. § 353a(a) and (c) (Supp. V 1999) unconstitutional.

Respectfully submitted,

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